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BAKER BOTTS L.L.P.
44TH FLOOR
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112-4498

EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/778,154	YOO, SEO HONG	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *138-148* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *138-148* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/17/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 138-148 are pending. Claims 149-151 were cancelled in the amendments to the claims, filed 5/17/2004. Claims 138-148 are examined.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/12/2005 has been entered.

Withdrawn Claim Rejections

3. The rejection of claims 138-147 and 148-150 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, are withdrawn in view of applicant's arguments, amendments to the claims and cancellation of claims 149-150, filed 5/17/2004.

4. The rejection of claim 151 under 35 U.S.C. 102(b) as anticipated by Nakazawa et al., (JP62153220, abstract only), is withdrawn as moot, in view of applicant's cancellation of said claim 151, filed 5/17/2004.

5. The rejection of claims 142-148 as unpatentable over the sole reference of Nakazawa et al., is withdrawn in view of applicant's arguments that Nakazawa et al. does not teach or suggest all elements of the claims 142-148. This rejection is

superseded by the rejection of claims 142-148 over Nakazawa et al., and Acharya et al., and Vandelli et al. See rejections under 35 U.S.C. 103(a).

Withdrawn Objections to the Claims

6. The objection to claim 139 for failing to further limit the subject matter of a previous claim, as set forth in the Final rejection, mailed 1/14, 2004, is withdrawn in view of applicant's amendment to said claim 139, filed 5/17/2004.

Election/Restrictions

7. Applicant's election, filed 9/23/2002, of Group VI, original claims 138-147, and the species of usodeoxycholic acid (Species Group I) and a starch conversion product (Species Group II) is again acknowledged and maintained. It is noted that the instant specification states:

> Based on these formulas, the aqueous solution dosage forms of various concentrations of certain bile acids (or salts) with its corresponding minimal quantity or more of high molecular weight aqueous soluble starch conversion products (for example; maltodextrin, liquid glucose, dried powder of liquid glucose (commercial corn syrup solid), dextran, dextrin, and soluble starch) or soluble non-starch polysaccharide (e.g. guar gum, pectin, gum arabic) were prepared.

Specification at p. 33, lines 7-12.

Priority

8. The instant application is a continuation-in-part of Serial No. 09/357,549, filed 7/20/1999, now US Patent 6,251,428, which claims benefit of 60/094,069, filed 7/24/1998; and claims benefit of US Provisional Application No. 60/180,268, filed 2/4/2000.

Information Disclosure Statement

9. The IDS filed 5/17/2004, has been fully considered.

Response to Amendment

10. The Declaration of Seo Hong Yoo (hereinafter "Yoo Declaration") filed on 5/17/2004 under 37 CFR 1.131 has been considered but is ineffective to overcome the reference of Japanese Patent No. JP62153220, abstract only, to Nakazawa et al., (also referred to as "Satoshi", i.e., the given name of second author Satoshi Hisano, by applicant and in the Yoo Declaration).

The Yoo Declaration reports a comparison between the methods taught in the instant application with the methods of the reference of Nakazawa et al. In evaluating the methods taught by Nakazawa et al., the Yoo Declaration, for example, states:

> (i) During preparation of the UDCA+amylodextin solution [paragraph 4(a)(i) above], the combination of the UDCA/ethanol mixture with 80 mL of water resulted in a milky solution. Upon heating, the solution with amylodextrin became mostly ***clear*** with some undissolved matter. After the solution cooled to room temperature, the solution appeared opalescent or turbid. The insoluble material settled to the bottom of the bottle with time. Substantial quantities of precipitation were visible at 24 weeks after the solution was prepared. After 3-4 months the ***clear*** solution (supernatant) again became cloudy and then, substantial precipitated material was observed at the bottom of the bottle at 4-5 months after the solution was prepared.. The presence of UDCA and amylodextrin in the precipitated material was confirmed by iodine test of amylodextrin, identification of UDCA with sulfuric acid & formalin, and HPLC. [Emphasis added]

Yoo Declaration at pp. 4-5, bridging paragraph. The Yoo Declaration states that "[t]he foregoing results demonstrate that the disclosures of Satoshi (otherwise known as Nakazawa et al.) are insufficient to enable the preparation of bile acid solutions that are stable for more than five months." Yoo Declaration at p. 12, paragraph 12.

The Yoo Declaration has been considered, but is not effective for overcoming the reference of Nakazawa et al. The examiner respectfully submits that the Yoo Declaration provides objective evidence that the solutions of Nakazawa et al. actually are "clear" solutions. The Yoo Declaration reports that said solutions of Nakazawa et al. are unstable after, for example, five months. However, the instant product claims do not recite a limitation that the products have a minimum time period for "stability" or, more to the point, for the property of being "clear". Thus applicant, in the reply to the previous Office action, relies upon the Yoo Declaration to show a limitation not recited in the claims (see below rejections under 35 USC §§ 102 and 103 (a)).

In the Yoo Declaration, clarity is assessed by eye. There would seem to be a degree of subjectivity to such an assessment. The practitioner might ask if a "clear" solution can also be "milky", "opalescent" or "turbid". It is well known in the art, of course, that absorption of light through a medium is described by the Lambert-Beer Law, and can be quantified by readily available instrumentation, such as a spectrophotometer. Indeed, the instant claims do not recite a range for the quality of being clear; *i.e.*, absorbance. Thus it is difficult to interpret the findings of the Yoo Declaration comparing the Nakazawa et al., reference to the instant claims.

Therefore, the examiner respectfully submits that the Yoo Declaration is ineffective to overcome Nakazawa et al. as a reference.

Specification

11. The amendment filed 7/3/2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment

shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

There is no support in the specification as filed for "aqueous soluble ~~sulfate~~ bismuth chelate" at p. 53, lines 1-5 (Example VIII).

There is no support in the specification as filed for "Bismuth ~~citrate~~ sulfate 5 g" at p. 53, lines 6-14.

There is no support in the specification as filed for "Bismuth ~~citrate~~ sulfate 5 g" at p. 53, line 19.

There is no support in the specification as filed for "Bismuth ~~citrate~~ sulfate 4 g" at p. 54, line 10.

There is no support in the specification as filed for "Bismuth ~~citrate~~ sulfate 4 g" at p. 55, lines 1-10.

There is no support in the specification as filed for "Bismuth sulfate 4 g" at p. 56, lines 1-9.

There is no support in the specification as filed for "Bismuth sulfate 4 g" at p. 57, lines 1-9.

There is no support in the specification as filed for "bismuth citrate as chelate" at p. 58, lines 1-5.

There is no support in the specification as filed for "Bismuth sulfate 10 g" at p. 60, line 9.

Applicant, in the Remarks filed 7/3/2003, states:

> The amendments to the specification made herein correct certain typographical and clerical errors and are fully supported by the

> specification as filed. Support for the amendments to Examples VIII, IX, X, XI, and XII are supported by, *inter alia*, the original Examples VIII, IX, X, XI, and XII respectively. For example, as originally filed, the description states that "[t]he formulations of Examples VIII, IX, and X include bismuth sulfate." Page 53, line 2. In addition, Examples XI and XII recite the addition of bismuth sulfate at page 56, lines 10-11 and page 57, lines 10-11 respectively. Support for the amendments to Examples XIII and XIV are supported by, *inter alia*, the original Examples XIII and XIV respectively. For example, one of ordinary skill in the art would recognize that the addition of bismuth citrate and citric acid would result in the formation of bismuth citrate as chelate in solution. Therefore, the specification amendments made herein do not constitute new matter.

Remarks at pp. 14-15, bridging paragraph.

Applicant's remarks have been considered but are not persuasive. In regards as to whether "one of ordinary skill in the art would recognize that the addition of bismuth citrate and citric acid would result in the formation of bismuth citrate as chelate in solution", the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness."). MPEP 2145.

In regards to the use of bismuth sulfate or citrate in specific amounts (e.g., "4 grams", "5 grams", "10 grams"), the specification as filed, does not provide support for the proposed amendments to the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

12. Claims 145-147 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for new matter.

Claims 145-147, added by amendment filed 1/8/2002, state the limitations "anticonvulsant activity", "an agent having prolonging survival time in hypoxic conditions", and "the group consisting of stomatitis, gingivoglossitis and toothache", respectively. There does not appear to be support for these limitations to the claims in the specification as filed. Applicant must point, with particularity, to where in the specification as filed, support for these limitations may be found.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

13. Claims 138-148 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "clear" in claims 138, its dependent claims, and 148, is a relative term that renders the claim indefinite. The term "clear" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of clearness or transparency or clarity, and one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Claims 138, its dependent claims and 148, recite the language "within a selected range of pH values", which renders the claims vague and indefinite, because the selecting the range of pH values would read on a mental step and does not define the range of the relevant physical property, so that one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed composition.

Claim 146 recites the language "an agent having prolonging survival time in hypoxic conditions", which renders the claim vague and indefinite, because said language does not make sense.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 138-141 are rejected under 35 U.S.C. 102(b) as being anticipated by Japan Publication No. 62153220, Formal Translation, (IDS filed 5/17/2004) to Shinzo Nakazawa and Satoshi Hisano (English translation of "Nakazawa et al."; also called "Satoshi" by the applicant and in the Yoo Declaration). It is noted that the Formal

Translation of Japan Publication No. 62153220 was the addendum to the Affidavit or Exhibits, filed 5/17/2004.

Claims 138-141 are drawn to a clear aqueous solution comprising; (i) a first material selected from the group consisting of an aqueous soluble bile acid salt, a bile acid conjugated with an amine by an amide linkage that is ursodeoxycholic acid (elected species), and combinations thereof; (ii) an aqueous soluble starch conversion product (elected species); and (iii) water, wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values.

Japan Publication No. 62153220, Formal Translation, (IDS filed 5/17/2004) throughout the publication and especially at p 2, teach a clear liquid agent (p. 2, para 2, claim 1 and para 3; which reads on a clear aqueous solution) comprising ursodeoxycholic acid or chenodeoxycholic acid (p. 2, para 2, claim 2) and a dextrin starch derivative that is maltodextrin, amylodextrin or erythrodextrin, (p. 2, claim 2, reading on an aqueous soluble starch conversion product (elected species)); and (iii) water (p. 2, claim 1), wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values (p. 9, para 16).

The Yoo Declaration is ineffective to overcome Nakazawa et al. as a reference for the reasons provided above in paragraphs 9 of the instant Office action. Briefly, the Yoo Declaration states that solutions prepared by the method of Nakazawa et al., provide solutions that do not remain clear for as long a duration (*e.g.*, after 5 months) as those of the instant application. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the

features upon which applicant relies (i.e., long-term clearness) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, the examiner respectfully submits that the Yoo Declaration is ineffective to remove the reference of Nakazawa et al. as prior art.

15. Claims 138-141 are rejected under 35 U.S.C. 102(b) as being anticipated by Panini et al., Pharmacological Research, Vol. 31, No. 3/4, 1995.

Claims 138-141 are drawn to a clear aqueous solution comprising; (i) a first material selected from the group consisting of an aqueous soluble bile acid salt, a bile acid conjugated with an amine by an amide linkage that is ursodeoxycholic acid (elected species), and combinations thereof; (ii) an aqueous soluble starch conversion product (elected species); and (iii) water, wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values.

Panini et al., throughout the publication, and especially at the abstract, p. 205, para 6-p. 206, para 5, p. 206, and Figure 1, teach dissolution of ursodeoxycholic acid with 2-hydroxypropyl-beta-cyclodextrin, which reads upon a solution within some selected pH value, comprising bile salt, an aqueous starch conversion product, and water. Absent evidence to the contrary, aqueous solutions wherein the bile acid and the starch conversion product are dissolved in water, will be "clear". See also rejection under 35 USC 112, second paragraph regarding the term "clear".

16. Claims 138-141 are rejected under 35 U.S.C. 102(b) as being anticipated by Wildauer, U.S. Patent No. 5,534,505.

Claims 138-141 are drawn to a clear aqueous solution comprising; (i) a first material selected from the group consisting of an aqueous soluble bile acid salt, a bile acid conjugated with an amine by an amide linkage that is ursodeoxycholic acid (elected species), and combinations thereof; (ii) an aqueous soluble starch conversion product (elected species); and (iii) water, wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values.

Wildauer, throughout the patent, and especially at col. 2, lines 1-60, teaches ursodeoxycholic acid in demineralized water, with beta-cyclo-dextrin, at pH values between 2.5 and 8, which meet the structural elements of the claimed invention and would therefore, absent evidence to the contrary, exist as a clear aqueous solution. See also rejection under 35 USC 112, second paragraph regarding the term "clear".

17. Claims 138-141 are rejected under 35 U.S.C. 102(b) as being anticipated by anticipated by Ventura et al., International Journal of Pharmaceutics, vol. 149, (1997), pp. 1-13.

Claims 138-141 are drawn to a clear aqueous solution comprising; (i) a first material selected from the group consisting of an aqueous soluble bile acid salt, a bile acid conjugated with an amine by an amide linkage that is ursodeoxycholic acid (elected species), and combinations thereof; (ii) an aqueous soluble starch conversion product

(elected species); and (iii) water, wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values.

Ventura et al, throughout the publication, and especially at p. 2, para 8, p. 7, para 2, p. 12, para 1-4 and Figure 7A and7B, teach ursodeoxycholic acid and beta-cyclo-dextrin, at pH value 1.1, dissolved in water-based solutions, which meet the structural elements of the claimed invention and would therefore, absent evidence to the contrary, exist as a clear aqueous solution. See also rejection under 35 USC 112, second paragraph regarding the term "clear".

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

18. Claims 138-147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Japan Publication No. 62153220 to Nakazawa et al., Formal Translation, (IDS filed 5/17/2004) and Acharya et al., US 6,210,699.

Claims 138-147 are drawn to a clear aqueous solution comprising; (i) a first material selected from the group consisting of an aqueous soluble bile acid salt, a bile acid conjugated with an amine by an amide linkage that is ursodeoxycholic acid (elected species), and combinations thereof; (ii) an aqueous soluble starch conversion product (elected species); and (iii) water, wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values. Claim

142 is drawn to a solution comprising one or more additional bile acids. Claims 143-147 are drawn to solution further comprising agents having anti-inflammatory activity, analgesic activity, or anticonvulsant activity, "an agent having prolonging survival time in hypoxic conditions" or an agent for alleviating or ameliorating stomatitis, gingivoglossitis or toothache. The terms, including "clear" and "an agent having prolonging survival time in hypoxic conditions" are interpreted as vague and indefinite (see the rejection of the these claims under 35 U.S.C. 112, second paragraph).

Japan Publication No. 62153220, Formal Translation, (IDS filed 5/17/2004), also known as the reference of Nakazawa et al., throughout the publication and especially at p 2, teach a clear liquid agent (p. 2, para 2, claim 1 and para 3; which reads on a clear aqueous solution) comprising ursodeoxycholic acid or chenodeoxycholic acid (p. 2, para 2, claim 2) and a dextrin that is maltodextrin, amylodextrin or erythrodextrin, (p. 2, claim 2, reading on an aqueous soluble starch conversion product (elected species)); and (iii) water (p. 2, claim 1), wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values (p. 9, para 16); and at p. 2, para 2, claim 2.

The Yoo Declaration is ineffective to overcome Nakazawa et al. as a reference for the reasons provided above in paragraphs 9 of the instant Office action. Briefly, the Yoo Declaration states that solutions prepared by the method of Nakazawa et al., (called "Satoshi" in the Yoo Declaration) provide solutions that do not remain clear for a long or indefinite period of time. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon

which applicant relies (i.e., permanent clarity or transparency) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, the Yoo Declaration is ineffective to remove the reference of Nakazawa et al. as prior art.

Acharya et al., US 6,210,699, throughout the patent, including the claims, disclose a device that includes drugs, and wherein:

> The device of the present invention is also suitable for transmucosally delivery of both ionic or non-ionic drugs for oral or systemic diseases including analgesics and anti-inflammatory agents (e.g. indomethacin, ibuproden), mouth disinfectants (chlorohexidine hydrochloride, hexylresorcine), enzymes (e.g. nitroglycerin, isosorbide dinitrate, nifedipine), antiasthmatics (e.g. disodium cromoglycate), antibiotics (e.g. penicillin, erythromycin), chemotherapeutics (e.g. sulfathiazole, nitrofurazone), local anesthetics (e.g. benzocaine), cardiotonics (e.g. digitalis, digoxin), antitussives and expectorants (e.g.codeine phosphate, isoproterenol hydrochloride), agents affecting digestive organs, antihistamines, antiinflammatory steroids, hemostatics, sex hormones, sedatives, antitumor agents, or the like. Effective amounts, i.e. from 2 to 20% by weight, of penetration enhancers such as a salt of a conjugate of a bile acid with taurine or taurocholic acid may be optionally added in the active layer to enhance the penetration of the active drug.

Acharya et al., US 6,210,699, col. 8, line 59-col. 9, line 10. Thus Acharya et al. teach adding penetration enhancers, such as bile acids with taurocholic acid, which is also a bile acid, so as to add one or more additional bile acids (as in claim 142) to agents that are analgesic, anti-inflammatory, sedatives (which read on anticonvulsants), antiasthmatics (which, absent evidence to the contrary, read on "an agent having prolonging survival time in hypoxic conditions") and mouth disinfectants (which read on agents for alleviating or ameliorating stomatitis, gingivoglossitis or toothache).

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have made clear aqueous solutions comprising a bile acid and a starch conversion product (as taught by Nakazawa et al.) and one or more additional bile acids, an aqueous starch derivative, water, and agents having anti-inflammatory activity, analgesic activity or anticonvulsant activity, "an agent having prolonging survival time in hypoxic conditions", or an agent for alleviating or ameliorating stomatitis, gingivoglossitis or toothache (as taught by Acharya et al.).

One of ordinary skill in the art would have been motivated to have made and used aqueous solutions comprising a bile acid and one or more additional bile acids, because Acharya teach bile acids as penetration enhancers, and teaches combining bile acid penetration enhancers with taurocholic acid, which is another bile acid, in order to facilitate delivery of the therapeutic agents. One of ordinary skill in the art would have been motivated to have made aqueous solutions comprising bile acids and starch derivatives with agents having anti-inflammatory activity, analgesic activity or anticonvulsant activity, "an agent having prolonging survival time in hypoxic conditions", or an agent for alleviating or ameliorating stomatitis, gingivoglossitis or toothache, because Acharya suggests combining such agents in bile acid containing solutions because bile acids are penetration enhancers, and because Nakazawa et al., teach combining bile acids with starch derivative to reduce the bitterness of the bile acid (Nakazawa et al, p. 3, para 03) and to produce a clear aqueous solution in which the bile acid was completely solubilized and in which there was no bitter taste (Nakazawa et al., p. 4, para 05), in order to facilitate delivery of known therapeutic agents.

19. Independent claim 148 is rejected under 35 U.S.C. 103(a) as being unpatentable over Japan Publication No. 62153220 to Nakazawa et al., Formal Translation, (IDS filed 5/17/2004) and Vandelli et al, International Journal of Pharmaceutics, vol. 118, (1995), pp. 77-83.

Independent claim 148 is drawn to a clear aqueous solution comprising; (i) a first material selected from the group consisting of an aqueous soluble bile acid salt, a bile acid conjugated with an amine by an amide linkage that is ursodeoxycholic acid; (ii) maltodextrin; and (iii) water, wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values; and wherein the weight ratio of maltodextrin to ursodeoxycholic acid is 25:1. The claim is interpreted as vague and indefinite in view of the rejection under 35 U.S.C. 112, second paragraph.

Japan Publication No. 62153220, Formal Translation, (IDS filed 5/17/2004), known as the reference of Nakazawa et al., throughout the publication and especially at p 2, teach a clear liquid agent (p. 2, para 2, claim 1 and para 3; which reads on a clear aqueous solution) comprising ursodeoxycholic acid or chenodeoxycholic acid (p. 2, para 2, claim 2) and a dextrin that is maltodextrin, amylodextrin or erythrodextrin, (p. 2, claim 2, reading on an aqueous soluble starch conversion product (elected species)); and (iii) water (p. 2, claim 1), wherein the first and second materials both remain in solution for all pH values of the solution within a selected range of pH values (p. 9, para 16); and at p. 2, para 2, claim 2, teaches a weight ratio of maltodextrin to ursodeoxycholic acid of 30:1 or higher.

The Yoo Declaration is ineffective to overcome Nakazawa et al. as a reference for the reasons provided above in paragraphs 9 of the instant Office action. Briefly, the Yoo Declaration states that solutions prepared by the method of Nakazawa et al., (called "Satoshi" in the Yoo Declaration) provide solutions that do not remain clear for a long or indefinite period of time. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., long-term clearness) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The Yoo Declaration is ineffective to remove the reference of Nakazawa et al. as prior art.

Vandelli et al., at p. 78, para 7, teach combining 1.7 g of a starch derivative, which is 2-hydroxypropyl-beta-cyclodextrin, with 487 mg of ursodeoxycholic acid (w/w ratio of 3.5:1) in a aqueous solution of a given pH.

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the art to have made clear aqueous solutions comprising maltodextrin to ursodeoxycholic acid in a weight ratio of 25:1.

One of ordinary skill in the art would have been motivated to have made and used aqueous solutions comprising maltodextrin to ursodeoxycholic acid in a weight ratio of 25:1 because Nakazawa et al. teach a weight ratio of maltodextrin to ursodeoxycholic acid of 30:1 and Vandelli et al. teach combining the starch derivative with ursodeoxycholic acid in a lower weight to weight ratio of 3.5:1, so that one of

ordinary skill in the art would have been motivated, in routine optimization, to decrease the maltodextrin to ursodeoxycholic acid weight ratio in a range from 30:1 to 3.5:1, thus encompassing the claimed value of 25:1.

Conclusion

20. Claims 138-148 are rejected.

21. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Higginbottom et al., International Journal of Pharmaceutics, vol. 109 (1994), pp. 173-180.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Mark L. Shibuya
Examiner
Art Unit 1639

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